

naturally occurring stem cells. To expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended claim 49 to incorporate the Examiner's suggestion. Applicants' amendment is not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of the rejection are respectfully requested.

2. Claims 32-33, 38, 41-42 and 49-60 are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey that, at the time the application was filed, Applicants had possession of the claimed invention. Specifically, the Office Action objects to the term "cellular composition", and alleges that the specification fails to provide support for this term. Applicants traverse this rejection to the extent it is maintained over the amended claims.

The standard for satisfying the written description requirement "is whether a claim defines an invention that is clearly conveyed to those of skill in the art at the time the application was filed." (MPEP 2163.02). However, the MPEP additionally reminds us that "[t]he subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement." (MPEP 2163.02). Accordingly, Applicants contend that the specification provides ample literal support to adequately describe the claimed subject matter.

Despite Applicants' contention that the specification provides ample support for the claim limitation "cellular composition", Applicants have amended the claim to further clarify the claimed subject matter. Literal support for Applicants' amendments can be found on pages 8 and 9 of the specification. Applicants' amendments are made solely for clarity and to expedite prosecution, and are not in acquiescence of the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of the rejection are respectfully requested.

3. Claims 32-33, 38, 41-47 and 49-60 are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, specifically for being overly broad in the recitation of "stem

cells.” Applicants maintain the arguments of record and contend that classifying the stem cells of the invention as “neuronal” does not limit the scope of the claims. The art contains a multitude of references which demonstrate that stem cells isolated from a given tissue may differentiate along previously unexpected lineages. Accordingly, classifying a stem cell as a neuronal stem cell simply because it is isolated from neuronal tissue or because it can differentiate along neuronal lineages is likely to be an incomplete classification at best.

Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended the claims to incorporate the Examiner’s suggestion. Applicants amendments are by no means in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

4. Claims 32-33, 38, 41-47 and 49-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants contend that the term “cellular composition” is art recognized, and one of skill in the art can readily recognize the metes and bounds of the claimed subject matter. This is the criteria for evaluating whether a claim complies with the requirements under 35 U.S.C. 112, second paragraph. Applicants remind the Examiner that a claim term need not explicitly appear in the disclosure in order for that claim to be definite. “The mere fact that a term or phrase used in the claims has no antecedent basis in the specification disclosure does not mean, necessarily, that the term or phrase is indefinite. There is no requirement that the words in the claim must match those used in the specification disclosure. Applicants are given a great deal of latitude in how they chose to define their invention so long as the terms and phrases used define the invention with a reasonable degree of clarity and precision.” (MPEP 2173.05(e)).

Applicants contend that one of skill in the art can readily recognize the metes and bounds of the claimed subject matter. Nevertheless, to expedite prosecution, Applicants have amended the claims to more particularly point out the claimed subject matter. Applicants’ amendments are made solely to expedite prosecution, and are not in acquiescence of the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

5. Claims 49-60 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Avoli et al. Applicants traverse this rejection to the extent it is maintained over the amended claims.

Applicants have previously argued and maintain that the brain slices of Avoli et al. contain a vast number of cell types which are not isolated from their complex microarchitecture. To further clarify the vast difference between the present invention and Avoli et al., Applicants have amended the claims to more explicitly describe the claimed composition of neural stem cells. Applicants' amendments are made solely to expedite prosecution, and Applicants reserve the right to prosecute claims of similar or differing scope. Applicants' amendments are believed to obviate the rejection, and reconsideration and withdrawal are requested.

6. Claims 32, 38, 43-47, 49, 53-57 and 59-60 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Sosnowski et al. as evidenced by Bruckenstein et al. Applicants traverse the rejection to the extent that it is maintained in light of the amended claims.

In accordance with MPEP 2131 and with the Courts, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the...claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Sosnowski et al. fail to satisfy the criteria clearly delineated by the MPEP and the Courts for anticipating the claimed invention. Applicants' claims are directed to cells isolated from peripheral tissue. The cells isolated by the methods of the present invention possess specific characteristics including: they are self renewing, express nestin, form non-adherent clusters, can differentiate to form neurons and/or glia, and can differentiate to form dopaminergic neurons. The cells disclosed by Sosnowski et al. fail to meet several of these limitations. For example, the cells of Sosnowski et al. do not express nestin, are not self renewing, and do not differentiate to form dopaminergic neurons. Accordingly, the cells disclosed by Sosnowski et al. do not anticipate Applicants' invention.

The Examiner has argued that although Sosnowski et al. fail to explicitly teach each and every limitation of the pending claims, the cells of Sosnowski et al. are inherently the same as

the presently claimed cells. However, Applicants point out that the MPEP and the Courts have established a very high threshold for rejecting claims based on characteristics which are allegedly inherently present in a prior art reference. "[T]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic."

"In re Rijckaert, 9 F.3d 1531, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. **Inherency, however, may not be established by probabilities or possibilities** (emphasis added). The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-1951 (Fed Cir. 1999) (The claims were drawn to a disposable diaper having three fastening elements. The reference disclosed two fastening elements that could perform the same function as the three fastening elements in the claims. The court construed the claims to require three separate elements and held that the reference did not disclose a separate third fastening element, either expressly or inherently.)"

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Applicants have cited several characteristics of the cells of the present invention which distinguish these cells from the cells taught by Sosnowski et al. Sosnowski et al. provide no evidence to demonstrate or suggest that the disclosed cells are self renewing, express nestin, or can differentiate to form dopaminergic neurons. Absent such specific evidence and absent specific guidance to suggest that the cells **would** possess these characteristics, Sosnowski et al. fail to satisfy the criteria for anticipating the presently claimed cells.

The Office Action has cited Bruckenstein et al. in an attempt to overcome the deficiencies of Sosnowski et al. Applicants maintain the arguments of record with regard to the combination of these references. Additionally however, Applicants point out that Bruckenstein et al. does not overcome other deficiencies of Sosnowski et al., as iterated in this response. Bruckenstein et al. neither demonstrate nor suggest that the specific cells taught by Sosnowski et al. are self renewing, express nestin, or can differentiate to form dopaminergic neurons.

Finally, in the last response, Applicants pointed out that the mere fact that the cells of Sosnowski et al. are isolated from the same region of the animal (the olfactory epithelium) is not evidence that the cells are inherently the same cells. Briefly, the heterogeneous nature of the cultures described in Sosnowski et al. demonstrate that the olfactory epithelium consists of a wide range of cell types (page 45, second column, as cited by the Examiner). Additionally, it was well established in the art, at the time the present invention was made, that a specific tissue may contain distinct populations of stem cells. For example, bone marrow was known to contain at least two types of stem cells which are distinct in terms of both their morphology and their gene expression profile: mesenchymal stem cells and hematopoietic stem cells. This argument further undermines any possible claim that the cells taught by Sosnowski et al. are inherently the same as the cells of the present invention, and yet was not addressed by the Examiner.

Applicants maintain that the cells of the present invention are not anticipated by the teachings of Sosnowski et al. The cells of Sosnowski et al. fail to meet each and every limitation set forth in the claims. Furthermore, Sosnowski et al. fail to provide any guidance to even suggest that the disclosed cells inherently possess the characteristics of the presently claimed cells. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

7. Claims 33 and 49 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Mayo et al. Applicants traverse this rejection to the extent it is maintained over the amended claims.

The basis of the rejection of claims 33 and 49 appears to be over an alleged ambiguity in the definition of the term "cellular composition" previously used to described the claimed subject matter. The Office Action appears to believe that this term is unclearly defined in the specification, and thus may be interpreted as reading on the tongue explant of Mayo et al. Applicants maintain that the tongue explant of Mayo et al. is not an isolated composition of stem cells because the cells are not isolated from the other cell types and the complex cytoarchitecture of the tongue explant. Mayo et al. simply provides an explant. Although this explant is isolated from its endogenous environment (i.e., it is only a piece of tongue – excised from the mouth in which it endogenously resides), the explant still maintains the complex cytoarchitecture and

multitude of cell types that comprise a tongue. Accordingly, the tissue of Mayo et al. fails to anticipate the claimed subject matter.

In addition to Applicants' arguments of record regarding the distinguishing characteristics of the claimed subject matter over Mayo et al., Applicants point out that the claims have been amended to more explicitly point out the features of the claimed neural stem cells. Applicants' amendments are not in acquiescence of the rejection but rather serve to more explicitly point out the features of the invention which have already been explicitly outlined in the specification. Applicants' amendments are believed to obviate the rejection, and reconsideration and withdrawal of the rejection are requested.

8. Claims 41 and 42 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Sosnowski et al. in view of La Salle et al. Applicants maintain the arguments of record with respect to this rejection, and contend that claims 41 and 42 are not unpatentable in view of the specific combinations of references cited by the Examiner. The Examiner has provided no motivation which would lead one of skill in the art to combine the cited references. The only motivation comes from the hindsight which allows one of skill in the art to **now** appreciate that it would be useful to combine the teachings of Sosnowski et al with those of La Salle et al. Such hindsight is an insufficient basis for rejecting the pending claims.

Despite Applicants' contention that the combined references do not anticipate claims 41 and 42, Applicants' have amended the claims thus obviating the rejection. Applicants' amendments are made solely to expedite prosecution of claims directed to commercially relevant subject matter, and are not in acquiescence of the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

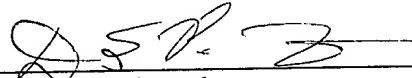
In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same

and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,

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